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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/630,319	07/31/2000	Arthur M. Krieg	C1039/7042	5464

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	19

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

F6

Office Action Summary	Application No. 09/630,319	Applicant(s) Krieg et al
	Examiner Jane Zara	Art Unit 1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Oct 3, 2002* .

2a) X This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *42-131* is/are pending in the application.

4a) Of the above, claim(s) *42-87, 102, and 105-131* is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) X Claim(s) *88-101, 103, and 104* is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____ .
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) X Information Disclosure Statement(s) (PTO-1449) Paper No(s). *3, 13, 16*
4) Interview Summary (PTO-413) Paper No(s).
5) Notice of Informal Patent Application (PTO-152)
6) Other:

DETAILED ACTION

Applicants' response filed October 3, 2002 and Sequence listing filed January 22, 2002 have been entered.

Response to Arguments

Withdrawn Rejections

Rejection of claim 104 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is hereby withdrawn in light of Applicants' arguments filed October 3, 2002, Paper No. 12.

Maintained Rejections

Claims 88-101, 103 and 104 are rejected under 35 U.S.C. 112, first paragraph, for lacking enablement over the scope claimed, for the reasons of record set forth in the Office action mailed March 28, 2002, Paper No. 9.

Applicant's arguments filed October 3, 2002 have been fully considered but they are not persuasive. Applicants argue that examples have been provided in the art that describe various examples of the in vivo administration of antisense oligonucleotides, and that these examples enable one skilled in the art to practice the instant invention over the scope claimed. Contrary to Applicants' assertions, the teachings provided by Bayever et al, Cossum et al and Agrawal et al do not enable one to practice the invention over the broad scope claimed. Bayever et al teach a lack of unexpected toxicity in 5 out of 6 subjects studied following a 10 day continuous infusion

of an antisense oligonucleotide into the patients. Bayever et al also teach a reduction of cumulative (leukemic) cell production in long term cell cultures obtained from a subset of the patients receiving this 10 day continuous infusion of antisense. But the authors are cautious in their interpretation of these in vitro results: "the cause of apparent decreased cell production remains unknown at this time" (See especially pate 389 of Bayever et al). Agrawal et al and Cossum et al teach stability studies of antisense oligonucleotides administered by various routes in vivo, comparing various modifications with antisense oligonucleotide stability. None of the references cited teach predictable efficacy of any antisense in treating or preventing a disease, condition or infections in an organism. The lack of toxicity in patients following a continuous 10 day infusion of antisense, and the enhance stability of modified forms of antisense oligonucleotides in animals are not representative of the ability to prevent and treat any and/or all bacterial infections in an organism comprising administration of (CpG containing) oligonucleotides.

Applicants argue that a detailed description of CpG immunostimulatory nucleic acids useful in treating immune deficiencies for treating and preventing bacterial infection has been provided in the instant disclosure (e.g. pages 15-17 of the specification), that actual working examples demonstrating B cell activation, NK activation and Th1 associated cytokine induction have been provided, and furthermore that one of skill in the art would have no reason to doubt a correlation between the data presented in the specification and the successful treatment and prevention of any and/or all bacterial infections in a subject. Contrary to Applicants' assertions, the various CpG containing sequences listed on pages 15-17, as well as the generic formulae

depicting a myriad of oligonucleotides, each containing at least one CpG dinucleotide, in combination with the increases in B cell and NK activation, as well as Th1 associated cytokine induction, do not provide enablement for the ability to treat and prevent any bacterial infection in a subject. The shift from a Th2 to a Th1 response demonstrated following the administration of a CpG oligonucleotide (of undisclosed sequence) arguably enhances various immune responses, but the increase in B or NK cell activation and the induction of various cytokine subsets following target cell exposure or target cell contact with a CpG-containing oligonucleotide of undisclosed sequence cannot be extrapolated to the ability to prevent any and/or all bacterial infections in any and/or all subjects. The prevention of bacterial infections would require the appropriate dosing and administration of an oligonucleotide (of a disclosed sequence beyond that provided in the instant disclosure, since the inclusion of the CpG motif within an oligonucleotide is necessary but not sufficient for generating predictable immune responses in an organism, including the complete prevention of any bacterial infection in an organism) whereby the appropriate cells are targeted in an organism that harbor any and/or all bacteria, and the appropriate cells are targeted in an organism whereby an immune response is elicited, and any and/or all bacterial infections are treated and prevented in that organism. Neither the activation of B or NK cells, nor the induction of Th1 associated cytokines, is representative of the successful prevention of any and/or all bacterial infections in any organism. Therefore, the scope of enablement rejection is maintained.

New Rejections

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 88-101, 103, 104 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 6-39 of U.S. Patent No. 6,207,646. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of USPN 6,207,646 are drawn to compositions and methods for treating a bacterial infection or for ameliorating an immune deficiency in an organism

comprising the enhancement of an immune response in an organism comprising the administration of a CpG containing oligonucleotide and the claims of the instant invention are drawn to compositions and methods for the treatment and prevention of bacterial infection in an organism comprising enhancing an immune response in an organism comprising the administration of immunomodulatory CpG containing oligonucleotides.

Claims 88-101, 103, 104 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,194,388. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of USPN 6,194,388 are drawn to compositions and methods for enhancing the immune response in an organism comprising the administration of CpG containing oligonucleotides and the claims of the instant invention are drawn to compositions and methods for the treatment and prevention of bacterial infection in an organism comprising the enhancment of an immune response in an organism comprising the administration of immunomodulatory CpG containing oligonucleotides.

Claims 88-101, 103, 104 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-49 of U.S. Patent No. 6,239,116. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of USPN 6,239,116 are drawn to compositions and methods for enhancing the immune response in an organism (including inducing IL-6 and IL-12 and stimulating natural killer cell lytic activity in an organism) comprising the administration of CpG

containing oligonucleotides and the claims of the instant invention are drawn to compositions and methods for the treatment and prevention of bacterial infection in an organism comprising the enhancement of an immune response in an organism comprising the administration of immunomodulatory CpG containing oligonucleotides.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ram R. Shukla

RAM R. SHUKLA, PH.D.
PATENT EXAMINER

JZ

February 24, 2003